

What is claimed is:

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1. A method to enhance long-term memory in a subject whose
5 cAMP-responsive gene expression is repressed due to
binding of a cAMP-response-element-binding-protein-2 to
a protein or a DNA associated with cAMP-responsive gene
expression, or both, which comprises administering to
10 the subject a compound capable of interfering with such
binding in an amount effective to interfere with
binding of the protein or the DNA so as to thereby
derepress cAMP-responsive gene expression in the
subject and enhance the subject's long-term memory.
2. The method of claim 1, wherein the compound is an anti-
15 cAMP-response-element-binding-protein-2 antibody.
3. The method of claim 1, wherein the compound is capable
of altering phosphorylation of the cAMP-response-
element-binding-protein-2.

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4. The method of claim 1, wherein the compound is an
organic compound, a peptide, a peptide mimetic, a small
molecule, or a nucleic acid.
- 25 5. The method of claim 1, wherein the protein associated
with cAMP-responsive gene expression comprises a cAMP-
response-element-binding-protein-1, a C/EBP protein, an
Aplysia ApC/EBP protein, a human C/EBP β protein, an AF-
1 protein, a c-jun protein, a fla protein, or a c-Fos
30 protein.
6. The method of claim 1, wherein the administration
comprises intralesional, intramuscular or intravenous

injection; infusion; liposome mediated delivery; viral infection; gene bombardment; topical, nasal, oral, anal, ocular, cerebro-spinal, or otic delivery.

- 5 7. A method for evaluating the ability of a compound to interfere with binding of a cAMP-response-element-binding-protein-2 to a protein associated with cAMP-responsive gene expression in a cell which comprises:
 - 10 (a) contacting the cell with the compound under suitable cell culture conditions;
 - 15 (b) measuring the amount of unbound protein associated with cAMP-responsive gene expression in the cell;
 - 20 (c) comparing the amount in step (b) with the amount of unbound protein associated with cAMP-responsive gene expression in the absence of the compound, so as to thereby evaluate the ability of the compound to interfere with binding of the cAMP-response-element-binding-protein-2 to the protein.
- 25 8. The method of claim 7, wherein the compound is an anti-cAMP-response-element-binding-protein-2 antibody.
- 30 9. The method of claim 7, wherein the compound is capable of altering phosphorylation of the cAMP-response-element-binding-protein-2.
10. The method of claim 7, wherein the compound is an organic compound, a peptide, a peptide mimetic, a small molecule, or a nucleic acid.

11. A method for evaluating the ability of a compound to interfere with binding of a cAMP-response-element-binding-protein-2 to a DNA associated with cAMP-responsive gene expression in a cell which comprises:

(a) contacting the cell with the compound under suitable cell culture conditions;

(b) measuring the amount of unbound DNA associated with cAMP-responsive gene expression in the cell;

(c) comparing the amount in step (b) with the amount of unbound DNA associated with cAMP-responsive gene expression in the absence of the compound, so as to thereby evaluate the ability of the compound to interfere with binding of the cAMP-response-element-binding-protein-2 to the DNA.

12. The method of claim 11, wherein the compound is an anti-cAMP-response-element-binding-protein-2 antibody.

13. The method of claim 11, wherein the compound is capable of altering phosphorylation of the cAMP-response-element-binding-protein-2.

14. The method of claim 11, wherein the compound is an organic compound, a peptide, a peptide mimetic, a small molecule, or a nucleic acid.

15. A method for treating a subject with a long-term memory defect due to binding of a cAMP-response-element-binding-protein-2 to a protein or a DNA associated with cAMP-responsive gene expression, or both, which

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comprises administering to the subject a compound capable of interfering with such binding in an amount effective to interfere with the binding of the protein or the DNA so as to thereby treat the subject's long-term memory defect.

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16. The method of claim 15, wherein the long-term memory defect comprises age-related memory loss, Alzheimer's Disease, amnesia, ischemia, shock, head trauma, neuronal injury, neuronal toxicity, neuronal degradation, Parkinson's disease, or senility.

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17. The method of claim 15, wherein the compound is an anti-cAMP-response-element-binding-protein-2 antibody.

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18. The method of claim 15, wherein the compound is capable of altering phosphorylation of the cAMP-response-element-binding-protein-2.

19. The method of claim 15, wherein the compound is an organic compound, a peptide, a peptide mimetic, a small molecule, or a nucleic acid.

20. The method of claim 15, wherein the protein comprises a cAMP-response-element-binding-protein-1, a C/EBP protein, an Aplysia ApC/EBP protein, a human C/EBP β protein, an AP-1 protein, a c-jun protein, a fla protein, or a c-Fos protein.

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21. The method of claim 15, wherein the cAMP-response-element-binding-protein-2 is human CREB2 transcription factor, murine ATF4 transcription factor, or Aplysia ApCREB2 transcription factor.

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- 5 22. The method of claim 15, wherein the administration comprises intralesional, intramuscular or intravenous injection; infusion; liposome mediated delivery; viral infection; gene bombardment; topical, nasal, oral, anal, ocular, cerebro-spinal, or otic delivery.
- 10 23. A recombinant eukaryotic cell comprising a DNA encoding a cAMP-response-element-binding-protein-2 not naturally present in the cell, operatively linked to a promoter capable of directed enhanced expression of the DNA, the DNA and the promoter being stably integrated into the genome of the eukaryotic cell.
- 15 24. A transgenic, non-human mammal whose somatic and germ cells contain and express a DNA encoding a cAMP-response-element-binding-protein-2 not naturally occurring in the non-human mammal, operatively linked to a promoter capable of directed enhanced expression of the DNA, the DNA and the promoter being stably integrated into the genome of the non-human mammal.
- 20 25. A pharmaceutical composition which comprises an effective amount of a compound capable of interfering with binding of a cAMP-response-element-binding-protein-2 to a protein associated with cAMP-responsive gene expression in a cell and a pharmaceutically acceptable carrier.
- 25 26. The pharmaceutical composition of claim 25, wherein the carrier is a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution, or a solid carrier.
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27. The pharmaceutical composition of claim 25, wherein the carrier comprises an appropriate adjuvant, a herpes virus, a liposome, a microencapsule, a neuronal cell receptor ligand, a neuronal-specific virus, a polymer encapsulated cell, or a retroviral vector.

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